## Remarks

Applicant requests reconsideration and withdrawal of the Final Rejection in the Official Action dated January 11, 2008 on the following grounds, alone or in combination:

- 1) The Final Rejection is premature; The sole grounds of rejection in the Official Action is a first action on the merits (obviousness) and has not been previously raised;
- 2) Examiner states that the action was made final as a result of Applicant's submission of an information disclosure statement (IDS) in Applicant's response of 10/10/07. This position must be in error because:
- a. a final rejection is improper where the new ground of rejection introduced by the Examiner after an IDS submission was <u>not</u> necessitated by amendment to the claims. (see MPEP 706.07(a); Examiner Note to 7.40.01). All amendments to the claims in the response of 10/10/07 were clarifications in response to s.112 rejections. No amendment changed the requirements for prior art searching. No amendment changed the subject matter to revert to previously considered arguments. No amendment suggested Applicant was stalling or delaying for time.
- b. the main reference cited in the obviousness rejection (Pitsch et al. 2001. Helv. Chem. Acta 84:3773-3795) was identified by the Examiner himself in the Examiner's search dated March 29, 2007. Therefore it was not a new reference in the IDS of 10/10/07. The secondary reference with which it is combined, Gunderson et al. (1989. Acta Chem. Scan. 43:706-709), though it was apparently first brought to Examiner's attention by the IDS of 10/10/07, is a general reference to silicon based chemical protecting groups. Gunderson et al. was not unavailable to the Examiner prior to the IDS. Therefore there is no basis to conclude that submission of the IDS "prompted" the new grounds of rejection.
- 3) As relates to the rejection of method claims 15 and 17, neither reference in the obviousness rejection remotely refers to the use of <u>2'-O-methylthiomethyl</u> modified ribonucleoside derivates, or any similar compound, thus the Final Rejection has not clarified the basis for the rejection of these claims, and provides nothing for Applicant to respond to.

Applicant therefore respectfully requests reconsideration and withdrawal of the Final Rejection.

In the event that withdrawal of the Final Rejection is not forthcoming, Applicant now responds to the Official Action.

Applicant has amended claim 8 to correct a typographical error. The claim illustrates a siloxymethyl derivate wherein Y is a suitable leaving group. This derivative is described in the specification, for example, at the last line of page 4. The noun "siloxymethyl derivative" correctly describes the moiety illustrated in the claim, thus correction of the typographical error in "siloxymethiderivative" is believed to be consistent with policy.

No other claims are amended.

Examiner has rejected claims 1-4, 8-10, 15 and 17 on the basis of obviousness under 35 U.S.C. S.103(a). Applicant traverses.

Examiner correctly notes that Pitsch et al. (2001. Helv. Chem. Acta 84:3773-3795) use a protecting group which does not have a tertiary carbon atom or hetero atom bound to the Siatom. Applicant presumes, based on Examiner's argument, that claims 5-7 and 11-14 relating to Si-hetero atoms are allowable because Siatoms bound to hetero atoms are not disclosed by Pitsch et al, and Examiner could find no reason to reject the claims related to Si-linked hetero atoms.

So Pitsch et al does not provide a basis to reject the Si-linked hetero atoms, how is it then that Pitsch et al. provides a *prima facie* basis for obviousness rejection of claims directed to a siloxymethyl derivative comprising a tertiary carbon?

Applicant agrees that Pitsch et al, and the corresponding Pitsch et al patent application publication WO1999009044 are directed to closely related subject matter, namely oligonucleotide synthesis using Si protecting groups. Yet neither Pitsch reference in any way identifies Si-atoms bound to a tertiary carbon atom. Because the Pitsch references relate to such similar subject matter, a strong presumption is raised that the authors were completely unaware of tertiary carbon atom substituents (as they were unaware of Si-hetero atom substituents). This suggests the Pitsch et al authors failed to appreciate the step that Examiner now considers 'obvious'. Stated otherwise, Examiner's view is that Pitsch et al failed to see their own work in the light of Gunderson et al. (1989. Acta Chem. Scan. 43:706-709), but that the law now requires the Examiner to draw that conclusion.

A better view is to recognize that Gunderson et al is not an appropriate secondary reference to create an obviousness rejection for Si-atoms bound to a tertiary carbon atom for use in nucleic acid synthesis. Gunderson et al. disclose in Scheme 1, a variety of compounds, among them compounds 4a and 4b, a chloromethoxysilane having a *tert*-butyl substituent on the Si-atom. This reference provides a role for these protecting groups in reactions for <u>sterically hindered alcohols</u>. There is a substantial theoretical and practical gap between reactions employing sterically hindered alcohols, and synthesis of 2'O modified nucleic acids. The use and value of these different compounds lie in separate fields, indeed in different disciplines. The failure of Pitsch to recognize that compounds 4a and 4b of the Gunderson reference could be applied to his discovery heavily suggests that the art of silyloxymethyl derivates was not nearly as advanced as Examiner believes. Gunderson is a very general reference which does not point the way to the inventive contribution that the Applicant has made with the instant patent application.

Considering the technical closeness of the Pitsch et al references to the instant application, it is important to recognize the evidence of non-obviousness they provide.

Applicant notes that the legal standard by which Examiner has evaluated obviousness is extremely loose stating "One would have had a reasonable expectation of success as the protecting groups are taught to be added and removed easily with normal reactions. Moreover, it is noted that the recent KSR decision forecloses the decision that a teaching/suggestion/motivation be found in the art."

Applicant notes that Examiner apparently acknowledges that there is no teaching/ suggestion/motivation (T/S/M) to combine the references he cites. This should be a strongly cautionary note for Examiner, because as stated recently in Ortho-McNeil Pharmaceutical v. Mylan Labs, No. 07-1223 (Fed. Cir. March 31, 2008) "...a flexible TSM test remains the primary guarantor against a non-statutory hindsight anlaysis...". The flexible TSM test "merely assures that the obviousness test proceeds on the basis of evidence – teachings, suggestions (a tellingly broad term), or motivations (an equally broad term) – that arise before the time of the invention as the statute requires."

Since there is no T/S/M to combine the references, what is left is Examiner's assertion that the objects of the instant invention could be derived from the Pitsch et al reference, in the light of Gunderson et al 'with a reasonable expectation of success', though this expectation of success arises without any motivation to combine the references. No action can be considered reasonable if there is no reason (or incentive) to do it. Examiner has merely asserted that the use of Gunderson protecting groups would be obvious to try without any reason to try it. The authors of Pitsch et al working in a closely related field failed to identify the invention now claimed by Applicants. Applicant fails to see how an obviousness rejection under 35 U.S.C. 103(a) can be supported on this basis.

Regarding method claims 15 and 17, Applicant has in the instant application provided an alternative synthetic method that takes advantage of the novel chemistry now claimed in the composition claims. As described in example 2 of the specification "Preparation of THEX building blocks via 2'-O-methylthiomethyl route", Applicants have provided a novel synthetic pathway which enhances the use of the compositions claimed in other claims. Examiner has provided no technical basis for the rejection of these claims, Applicant therefore respectfully requests further explanation of the rejection.

Finally, in the event that withdrawal of the Final Rejection is not forthcoming, Applicant submits herewith by separate paper, a Notice of Appeal of the final rejection of claims.

Respectfully submitted,

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